

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 24 JUL 2006

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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:
DEBORAH A. SOMERVILLE
KENYON & KENYON
ONE BROADWAY
NEW YORK, NY 10004

Date of mailing
(day/month/year) **20 JUL 2006**

Applicant's or agent's file reference

11245/53476

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/US04/43482

International filing date (day/month/year)

20 December 2004 (20.12.2004)

Priority date (day/month/year)

19 December 2003 (19.12.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC: **A61K 38/00(2006.01)**

USPC: 514/12

Applicant

IMCLONE SYSTEMS INCORPORATED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (571) 273-3201

Date of completion of this opinion

23 June 2006 (23.06.2006)

Authorized officer

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US04/43482

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed
- ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☐ a sequence listing
- ☐ table(s) related to the sequence listing

b. format of material

- ☐ on paper
- ☐ in electronic form

c. time of filing/furnishing

- ☐ contained in the international application as filed.
- ☐ filed together with the international application in electronic form.
- ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US04/43482

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>13, 14, 22-24, 26</u>	YES
	Claims <u>1-9, 11, 12, 15-21, 25</u>	NO
Inventive step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-26</u>	NO
Industrial applicability (IA)	Claims <u>1-26</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-9, 11, 12, 15-19, and 25 lack novelty under PCT Article 33(2) as being anticipated by US 20030203844 (Delfani et al) 30 October 2003. The reference teaches methods of treatment of CNS disorders using reagents that modulate the proliferation, migration, differentiation and survival of central nervous system cells (see Abstract). The reagents taught include FGF2 [0338], VEGF (whole document), and neural stem cells propagated ex vivo [0035]. The effect of modulating the migration of neural progenitor cells recited in the instant claims merely reflects a newly discovered inherent property; this outcome would occur whenever the methods taught in the prior art are practiced.

Claims 20, 21, and 25 lack novelty under PCT Article 33(2) as being anticipated by US Patent 6261585, 17 July 2001. The reference teaches incorporation in of VEGF and bFGF into biocompatible polymers for in vivo implantation (column 3, lines 35-50), thereby anticipating claims 20, 21, and 25.

Claim 10 lacks an inventive step under PCT Article 33(3) as being obvious over US 20030203844. If one aims to use undifferentiated stem cells, it would be obvious to pick cells that do not express known markers of differentiation.

Claims 13, 14, 22-24, and 26 lack an inventive step under PCT Article 33(3) as being obvious over US 20030203844 in view of US Patent 626158. As noted, US 20030203844 teaches treatments using VEGF, FGF2, and neural stem cells and US Patent 6261585 teaches the use of these elements in biocompatible matrices. The instant claims recite the obvious combination of these elements.

Claims 1-26 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/43482

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

Application No.
Patent No.

Publication date
(day/month/year)

Filing date
(day/month/year)

Priority date (valid claim)
(day/month/year)

2. Non-written disclosures (Rules 43bis.1 and 70.9)

Kind of non-written disclosure

Date of non-written disclosure
(day/month/year)

Date of written disclosure referring to
non-written disclosure
(day/month/year)